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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 04/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/963,693	RUVKUN ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) *4-6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 1/23/04 has been acknowledged.

Claim 2 is amended.

Claims 4-6 are withdrawn

Claims 1-3 are pending and are examined in this office action.

This application contains claims 4-6 drawn to an invention nonelected with traverse in Paper No. 1/23/04. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

*Applicants are required to follow Amendment Practice under revised **37 CFR §1.121**. The fax phone numbers for the organization where this application or proceeding is assigned is **703-872-9306**.*

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Claim Rejections - 35 USC § 102

Claim 2 is rejected under 35 U.S.C. 102(b) as being anticipated by Myers et al (PNAS 94:9052-9057, 1997) for the same reasons of record as set forth in the office action mailed on 08/21/03.

Myers teaches that PTEN is a tumor suppressor gene identified on chromosome 10. The cited art further teaches that PTEN, which is located on locus 10q22-23 is deleted or mutated in a significant fraction of **glioblastomas** and **prostrate tumors**. The cited art further teaches that germ line mutation in PTEN gene give rise to Cowden disease which is associated with the formation of multiple benign tumors and increases susceptibility to malignant cancers (page 9052, col.1-2). The cited art further teaches

phosphatase assays to evaluate PTEN activity (page 9053 col.2 para 2). The cited art further teaches evaluation of PTEN related phosphatase activity in various PTEN mutants (page 9055, col.1 para 2; page 9056, fig-4, fig-5). The cited art further teaches that a point mutation discovered in a glioma sample that changes Leu57-Trp (L57W) eliminates PTEN phosphatase activity (page 9056, col.2 para.2). The cited art further teaches that loss of PTEN activity leads to progression of cells to a cancerous state. The cited art further establishes a correlation between the severity in the disruption of PTEN activity and the pathology[1] of diseases (The scientific study of the nature of disease and its causes, processes, development, and consequences) like Bannayan-Zonana and Cowden disease (page 9057, col.1 para.3). Given the broadest reasonable interpretation the development of a cancer or tumors has inherently been associated with decreased longevity in a patient. Thus the cited art clearly anticipate the invention as claimed.

Response to arguments

The applicant argues that the claim 2 has been amended to recite "the normal logevity of a patient". The applicant argues that the normal life span differs from the likelihood that a patient will prematurely develop cancer due to the absence of PTEN tumor suppressor activity. The applicant argues that the office has incorrectly equated rate of aging with the statistical likelihood that a patient will develop a disease. The applicant argues that the Myers reference which is limited to a discussion of PTEN'S role in disease susceptibility cannot be anticipatory to a claim directed to the diagnosis of the rate of normal aging. The applicant argues that even though a PTEN mutation results in the development of a malignancy, this does not satisfy the standard for inherency.

However, applicant's arguments are found NOT persuasive. The cited art clearly teaches that PTEN, which is located on locus 10q22-23 is deleted or mutated in a significant fraction of **glioblastomas** and **prostrate tumors**. In addition the cited art teaches that establishes a correlation between the severity in the disruption of PTEN activity and the pathology of diseases like **Bannayan-Zonana** and **Cowden disease** (page 9057, col.1 para.3). The office has clearly provided the evidence that the development of glioblastomas, prostrate tumors Bannayan-Zonana and Cowden

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[1] *The American Heritage® Dictionary of the English Language, Third Edition* copyright © 1992 by Houghton Mifflin Company.

disease are related to diminished PTEN phosphatase activity. For example, a point mutation discovered in a glioma sample that changes Leu57-Trp (L57W) eliminates PTEN phosphatase activity (page 9056, col.2 para.2). Development of a malignant cancer in general is associated with a pathological state, which inherently affects the life span of a cancer patient, which is less than average life span in humans. Thus the cited art clearly establishes that decease in PTEN expression or activity is associated with development of cancers, which in turns decrease the longevity in PTEN associated cancer patients.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Myers et al (PNAS 94:9052-9057, 1997 as applied to claim 2 above, and further in view of Maehama et al (J Biol. Chem. 237(22):13375-13378, 1998) for the same reasons of record as set forth in the office action mailed on 08/21/03.

Myers teaches that PTEN is a tumor suppressor gene identified on chromosome 10. The cited art further teaches that PTEN, which is located on locus 10q22-23 is deleted or mutated in a significant fraction of glioblastomas and prostrate tumors. The cited art further teaches that germ line mutation in PTEN gene give rise to Cowden disease which is associated with the formation of multiple benign tumors and increases susceptibility to malignant cancers (page 9052, col.1-2). The cited art further teaches phosphatase assays to evaluate PTEN activity (page 9053 col.2 para 2). The cited art further teaches evaluation of PTEN related phosphatase activity in various PTEN mutants (page 9055, col.1 para 2; page 9056, fig-4, fig-5). The cited art further teaches that a point mutation discovered in a glioma sample that changes Leu57-Trp (L57W) eliminates PTEN phosphatase activity (page 9056, col.2 para.2). The cited art further teaches that loss of PTEN activity leads to progression of cells to a cancerous state. The cited art further establishes a correlation between the severity in the disruption of PTEN activity and the pathology[2] of diseases (The scientific study of the nature of disease and its causes, processes, development, and consequences) like Bannayan-Zonana and Cowden disease (page 9057, col.1 para.3). Given the broadest reasonable interpretation the development of a cancer ot tumors has inherently been associated with decreased longevity in a patient. However, Myers does not teach evaluation of expression or activity of PTEN by analyzing a lipid phospatase activity.

Maehama teaches the tumor suppressor, PTEN/MMAC1, dephosphorylates the lipid second messenger, phosphatidylinositol 3,4,5-trisphosphate (PtdIns(3,4,5)P_3). The cited art further teaches that PtdIns(3,4,5)P_3 is a key molecule involved in cell growth

signaling. The cited art teaches that the PTEN catalyzed dephosphorylation of PtdIns(3,4,5)P_3, specifically at position 3 on the inositol ring. (see abstract). The cited art further teaches that PTEN has tumor suppressive activity (col.1 para.1). The cited art further teaches further teaches a method of determining PtdIns(3,4,5)P_3 in a biological sample comprising human 293cells (Page 13375, col.2 para.3). In addition the cited art further teaches a method of determining PI 3-kinase activity (Page 13375, col.2 para.4

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the method as taught by Myers by substituting the substrate of PTEN with PtdIns(3,4,5)P_3. One would have been motivated to do so because PTEN has been known to encode the active site consensus motif HCXXGXR(S/T) found in all (protein-tyrosine phosphatases (PTPases) that elicits phosphoinositide phosphatase activity. One would have a reasonable expectation of success since PTEN has been known to catalyze the dephosphorylation of PtdIns(3,4,5)P_3 specifically through position 3 on the inositol ring. Thus the invention as claimed is prima facie obvious in view of cited prior art of record.

Response to arguments

The applicant argues that Myers fails to teach or suggest a role for PTEN in longevity. The applicant further argues Maehama merely characterizes the enzymatic activity of recombinant PTEN and fails to teach or suggest that PTEN functions in mammalian longevity. The applicant concluded that the combined teaching of Myers and Maehama does not teach the claimed diagnostic method.

However, applicant's arguments are found NOT persuasive. Mayers clearly teaches that a mutation in PTEN gene is not only associated with development of **glioblastomas** and **prostrate tumors** but play a role in the development of malignancies associated with **Bannayan-Zonana** and **Cowden disease**. Development of a malignant cancer in general is associated with a pathological state, which inherently affects the life span of these patients. Thus the cited art clearly establishes that decease in PTEN expression or activity is associated with decrease in logevity. Furthermore Maehama teaches that the PTEN has tumor suppressive activity (col.1 para.1). Maehama teaches that PTEN catalyzed dephosphorylation of PtdIns(3,4,5)P_3, specifically at position 3 on the inositol ring. In addition the cited art clearly teaches a method of determining PtdIns(3,4,5)P_3 in a biological sample comprising human 293cells (Page 13375, col.2 para.3).

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the method as taught by Myers by substituting the substrate of PTEN with PtdIns(3,4,5)P_3. One would have been motivated to do so because PTEN has been known to encode the active site consensus motif HCXXGXR(S/T) found in all (protein-tyrosine phosphatases (PTPases) that elicits phosphoinositide phosphatase activity. One would have a reasonable expectation of success since PTEN has been known to catalyze the dephosphorylation of PtdIns(3,4,5)P_3 specifically through position 3 on the inositol ring. Thus the invention as claimed is prima facie obvious in view of the combined teaching of cited prior art of record.

Claim Rejections - 35 USC § 112

Claims 1 and 3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the same reasons of record as set forth in the office action mailed on 08/21/03.

Nature Of Invention:

Invention relates to a method of diagnosing **impaired glucose tolerance condition** and **obesity** in a patient.

Breadth Of Claims And Guidance Provided By The Inventor:

The instant claims are drawn to a method of diagnosing impaired glucose tolerance condition, obesity and longevity in a patient by analyzing the level of PTEN expression or activity in a sample isolated from patient by measuring PTEN related any and all lipid phosphatase activity. The specification teaches Daf-18 maps to a genetic region which bears the probable C. elegans homologue (T07A9.6) of the tumor suppressor gene PTEN. Consistent with the role of PTEN as a daf-18 homologue is the fact that PTEN has lipid phosphatase activity that dephosphorylates position 3 on the inositol ring of PIP3 in vitro and decreases the levels of the lipid products of PI3K in response to insulin signaling in human 293 cells. The applicant hypothesized that a decrease in PTEN activity would be predicted to enhance PI3K signaling, consistent with daf-18 activity (spec. page 108, lines 9-22). At best the specification only disclosed a C.elegans model wherein the interaction of various daf-proteins in the regulation of glucose metabolism and longevity has been studied (spec pages 108-117). The specification further disclosed that PTEN and C.elegans daf-18 have very limited sequence similarity (spec. fig-39B). The specification further hypothesized that PTEN on

chromosome 10 is a candidate gene for human autosomal dominant type II diabetes as well as for human longevity control. Reduction in PTEN activity would be expected to potentiate insulin and/or insulin-like growth factor signaling, but an increase of PTEN activity would be expected to cause insulin resistance downstream of the insulin receptor, the type observed in late onset diabetes. However the specification as failed to establish the role of PTEN in mammalian glucose homeostasis.

State Of Art And Predictability:

The state of the art at the time of filing teaches that the development of impaired glucose tolerance and obesity is multi-factorial and complex. Obesity and type 2 diabetes are the most prevalent and serious metabolic diseases that are associated with a chronic inflammatory response characterized by abnormal cytokine production, increased acute-phase reactants and other stress-induced molecules. Many of these alterations seem to be initiated and to reside within adipose tissue, an unusual site for inflammation. Elevated production of tumour necrosis factor (TNF)-α by adipose tissue decreases sensitivity to insulin and has been detected in several experimental obesity models and obese humans. Free fatty acids (FFAs) are also implicated in the etiology of obesity-induced insulin resistance, although the molecular pathways involved in their action remain unclear (Hirosumi et al. Nature.420(6913):333-6 2002). Even though activation of PI3K is necessary for full stimulation of glucose transport by insulin, emerging evidence suggests that it is not sufficient and another pathway may also be necessary. The signals downstream of PI3K are still unknown, and there is controversy as to whether the serine/threonine kinase Akt/protein kinase B (PKB) or the protein kinase C (PKC) isoform λ/ζ mediates insulin stimulation of glucose transport. The pathways that mediate insulin's metabolic effects diverge downstream of PI3K and show differential sensitivity to varying levels of insulin (Khan et al. J. Clin. Invest. 106(4):473-481, 2000 page 473, col.2, page 475, fig-1). Furthermore, insulin resistance in obesity and type 2 diabetes is manifested by decreased insulin-stimulated glucose transport and metabolism in adipocytes and skeletal muscle and by impaired suppression of hepatic glucose output caused by downregulation of the major insulin-responsive glucose transporter, GLUT4 (Khan page 474 co.1, para.1). In addition FFA, leptin and TNF-α are other likely candidates that are know to affect glucose homeostasis (Khan page 474 col.2, page 476 fig-2). Furthermore, under hyperglycemic, hyperinsulinemic conditions, muscle glycogen synthesis is the major pathway for glucose metabolism in both normal and diabetic individuals, wherein the defective muscle glycogen synthesis plays a major role in causing insulin resistance in patients with type 2 diabetes. Defects in glycogen synthase, hexokinase II, and glucose transport have also been implicated in the loss of muscle glycogen synthesis in type 2 diabetics. In addition increased plasma free fatty acid concentrations are typically associated with many insulin-resistant states, including obesity and type-2 diabetes mellitus (Shulman J Clin. Invest. 106:171-176, 2000, see page 171 col.2 para.2, page 172 col.2 para.3; fig-2). In addition, obesity is a complex phenotype which is not only the result of genetic variations but is also the out come of personal behavioral and life style (Lonnqvist et al Nat. Med. 1(9):950-953, 1995, see page 951 col.1 para.1 line 1). Obesity appears to lessen life expectance markedly especially among young adults (Fontaine et al JAMA 289:187-193, 2003). Therefore

considering the applicant's disclosure it is even unclear how one skill in the art would conclude that increase in PTEN activity that causes obesity would not leads to decreased longevity or visa versa (especially in context of invention as claimed in claim 2). The state of the art a the time of filing was such that it has been unclear whether the PTEN (daf-18) activity is regulated during insulin-like signaling or any other signaling activity, since PTEN lipid phosphatase activity is low in vitro due to a missing modification by the insulin signaling cascade (Ogg et al, Mol Cell 2:887-893, 1998). Since the factors that affect PTEN activity in vivo are not well understood it is unclear what would be a representative control sample that can be used to evaluate the claimed PTEN activity. In addition it is unclear how one skill in the art would diagnose impaired glucose tolerance condition or propensity thereto by analyzing PTEN lipid phosphates activity alone in type-I diabetic patients, wherein the impaired glucose tolerance is the result of loss of insulin secretion. Thus considering the limited amount of guidance provided in the specification as filed and the state of art at the time of filing one skill in the art would have to engage in excessive and undue amount of experimentation to establish role of PTEN in glucose homeostasis.

Response to arguments

The applicant argues that specification teaches that PTEN modulates mammalian insulin signaling, just as C elegans Daf-18 modulates insulin signaling in the worm. The applicant argues that the specification disclosed that a significant parallel exist between C. elegans and mammalian insulin signaling. Citing a post filing publication (Butler et al. Diabetes 51:1028-1034, 2002) the applicant argues that PTEN modulates mammalian insulin signaling just as the applicant disclosed. Discussing Hirosumi, Shulman and Lonnqvist the applicant argues that these references fail to address the possible use of PTEN level or activity in diagnosing an impaired glucose tolerance condition. In response to Office's assertion that the claimed methods of diagnosing obesity and longevity are contradictory the applicant argues that it does not logically follow, nor do applicants teach, that any decrease in the level of PTEN would necessarily result in a decrease in longevity. The applicant argues that claimed diagnostic method requires that the decreases or increase in PTEN levels which are relative to a control sample. The applicant admits that given that obesity has a devastating impact on human health and life expectancy, the skilled artisan reading Applicants' disclosure understands that such methods would likely improve human health and increase longevity.

However, applicant's arguments are found NOT persuasive. Applicant's argument alone cannot take place of evidence lacking in the record (see In re Scarbrough 182 USPQ, (CCPA) 1979). Besides a hypothetical model, the specification as filed fails to provide a single working example, which establishes that PTEN modulates mammalian insulin signaling. Under the law, the disclosure "shall inform how to use, not how to find out how to use for themselves." See In re Gardner 475 F.2d 1389, 177 USPQ 396 (CCPA 1973). Applicant's argument that Butler et al. (Diabetes 51:1028-1034, 2002) teaches that PTEN modulates mammalian insulin signaling just as the applicant disclosed has been found unpersuasive because each patent application is examined on its own merit and is considered enabled in view of its own disclosure. The issue is not whether the other application support their claims but whether one supports its claims "[i]t is immaterial whether similar claims have been allowed to other" In re Gialito 188USPQ 645,648 (CCPA 1976). Considering the state of the art the specification as filed fails to provide a single working example, which establishes that PTEN modulates mammalian insulin signaling.

Hirosumi, Shulman and Lonnqvist clearly reflect the state of the art teaching that development of impaired glucose tolerance and obesity is multi-factorial and complex. The earlier office action clearly provides the evidence, which establishes the unpredictability tin the art. For example, Even though activation of PI3K is necessary for full stimulation of glucose transport by insulin, emerging evidence suggests that it is not sufficient and another pathway may also be necessary. The signals downstream of PI3K are still unknown, and there is controversy as to whether the serine/threonine kinase Akt/protein kinase B (PKB) or the protein kinase C (PKC) isoform λ/ζ mediates insulin stimulation of glucose transport. The pathways that mediate insulin's metabolic effects diverge downstream of PI3K and show differential sensitivity to varying levels of insulin (Khan et al. J. Clin. Invest. 106(4):473-481, 2000 page 473, col.2, page 475, fig-1). The applicant fails to consider the complexities involved in the mammalian insulin signal transduction pathway especially in context with impaired glucose tolerance and the development obesity. The applicants argument that the claimed diagnostic method requires that the evaluation of PTEN levels relative to a control sample has been found

unpersuasive because the factors that affect PTEN activity in vivo are not well understood it is unclear what would be a representative control sample that can be used to evaluate the claimed PTEN activity. In addition it is unclear how one skill in the art would diagnose impaired glucose tolerance condition or propensity thereto by analyzing PTEN lipid phosphates activity alone in type-I diabetic patients, wherein the impaired glucose tolerance is the result of loss of insulin secretion. Considering the unpredictability in the state of art the specification even fails to define what encompasses a control sample, which can be used to assess variation in the level of PTEN expression and/pr activity.

It is noted that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable (*See Brenner v. Manson , 383 U.S. 519, 536, 148 USPQ 689, 696 (1966), Stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion"*) Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

In instant case the specification as failed to establish the role of PTEN in mammalian glucose homeostasis and/or obesity. Diagnosis of impaired glucose tolerance condition and obesity by analyzing any and all kind of PTEN lipid phosphatase activity in any and all tissues sample is not considered routine in the art and without sufficient guidance to role or PTEN in glucose homeostasis and/or obesity, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore considering the unpredictability in the art and the limited guidance provided in the specification as filed one skill in the art would have to engage in excessive and undue

amount of experimentation to exercise the invention as claimed. The undue experimentation required would include scientific evaluation of the role of PTEN in impaired glucose tolerance and obesity especially in context with the multi factorial nature of these disorders.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "the normal longevity of a patient" in claim 2 is a relative term, which renders the claim indefinite. The term " the normal longevity of a patient " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

The fax phone number for the organization where this application or proceeding is assigned is **703-872-9306**. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sumesh Kaushal Ph.D.
Examiner Art Unit 1636

JEFFREY FREDMAN
PRIMARY EXAMINER